CASO CLÍNICO

Transverse myelitis and chronic urticaria in systemic lupus erythematosus. Case report

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We report a 40 years old woman with chronic urticaria and acute transverse myelitis associated with systemic lupus erythematosus. The urticaria appeared in her adolescence and after 26 years was followed by photosensitivity, peripheral polyarthritis and acute transverse myelitis, with positive antiphospholipid and antinuclear antibodies. Both chronic urticaria and acute transverse myelitis have been described associated with or appearing as the first manifestation of systemic lupus erythematosus. Transverse myelitis is a rare and still poorly understood condition reported in about 2% of patients with systemic lupus (Rev Méd Chile 2005; 133: 209-13).

(Key Words: Lupus erythematosus, systemic; Myelitis, transverse; Urticaria)

Mielitis transversal y urticaria crónica en el lupus eritematoso sistémico

Se relata un caso de urticaria crónica y mielitis transversal aguda en asociación con lupus eritematoso sistémico en una mujer de 40 años. La urticaria se inició en su adolescencia y, después de 26 años, presentó fotosensibilidad, poliartritis, meningitis aséptica y mielitis transversal aguda, con anticuerpos antifosfolípidos y antinucleares positivos. Se ha descrito urticaria crónica y mielitis transversal en asociación, o como la primera manifestación del lupus eritematoso sistémico. La mielitis transversal es una condición rara y poco comprendida, diagnosticada en cerca de 2% de los pacientes con lupus eritematoso sistémico y, muy frecuentemente asociada con anticuerpos antifosfolípidos. Los autores describen un caso de esta rara asociación y resaltan la necesidad de evaluaciones sistemáticas del diagnóstico en pacientes con urticaria crónica, porque esta condición suele ser una manifestación cutánea de enfermedades sistémicas, la puede anteceder por mucho tiempo y dificultar la correcta caracterización del lupus eritematoso sistémico, correlacionado a la usual corticoterapia prolongada.

Recibido el 16 de julio, 2004. Aceptado en versión corregida el 3 de noviembre, 2004.

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Transverse myelitis (TM) is a rare and still poorly understood condition reported in 1-2% of patients with systemic lupus erythematosus (SLE), and is associated with the presence of antiphospholipid antibodies (aPA)¹. The diagnosis of SLE must be discarded in patients with chronic urticaria, because urticariform lesions may occur associated with collagen diseases^{2,3}.

Although without clear distinction among the acute and chronic forms and the urticarial vasculitis, Yell JA et al (1966), described occurrence of urticaria in 44% of 73 patients with SLE⁴. In the study of López de Maturana et al, 72% of 32 patients with pathological diagnosis of cutaneous vasculitis were women, with a mean age of 43.5 years, and palpable purpura, erythematous macules and urticaria were the most frequently observed skin lesions, while connective tissue diseases and systemic vasculitis were the most commonly associated diseases⁵. Noteworthy, those authors did not find fibrinoid necrosis in 59.4% of their cases associated with systemic diseases and autoimmune disorders, including systemic vasculitis, rheumatoid arthritis, progressive systemic sclerosis and SLE⁵. As autoimmunity also plays an important role in the development of chronic urticaria associated with SLE^{2,4,6} and both conditions may be influenced by the use of corticosteroids, the correct characterization of SLE can result delayed or mistaken, favouring eventual diagnostic pitfalls.

We describe a case of TM and aPA positive in a middle-aged woman with SLE, in whom the urticaria was treated with corticosteroids during 26 years before the characterization of this collagen disease. Both, urticaria and TM may constitute an early manifestation of SLE^{1,7}.

CASE REPORT

A 40 years old Brazilian housewife attended to hospital complaining of non-scarring alopecia and ascending paresthesia and paraparesis in the lower limbs which rapidly evolved to paraplegia. She also referred urinary and bowel dysfunction. Beginning at the age thirteen (1976), she related episodes of itching and fugacious reddish papules

and plaques in the skin soon after hot baths. Since 28 years of age, these lesions have been recurring at yearly intervals, persisting for 3 to 12 months in spite of the use of corticosteroids and hydroxyzine. Two years later, she noticed photosensitivity and, at 36 years, a spontaneous abortion occurred. In 2002, she developed recurrent headaches and migratory arthralgia involving the temporomandibular, elbow, wrist, metacarpophalangeal, interphalangeal, coxofemoral, knee, ankle and metatarsophalangeal joints, in addition to episodes of asymmetric peripheral polyarthritis, coinciding with a positive HEp-2 rim ANA indirect immunofluorescence test.

On admission, she was conscious and well-oriented, with Cushingoid facies and urticaria lesions (Figure 1) predominantly on the trunk. Body mass index: 25.3 kg/m². Skin temperature was 36.5°C. The heart was rhythmic, 88 bpm, and there were no murmurs. Blood pressure: 140/90 mmHg. The lungs were clear and the respiratory rate 20 ipm. There was a discrete abdominal distension and tympanism, with bilateral sensory abolition below the epigastrium level. The liver and spleen were normal, and there was leg weakness and muscle flaccidity, with ankle jerk and plantar hyporeflexia, mainly on the right side.

Erythrocyte count 4.65 x 10⁶/mm³, hemoglobin 13.4 g/dl, hematocrit 41.5%, mean cell volume 89.2 fl, leukocyte count 17,500/mm³ (neutrophils: bands 11%, segmented 83%, eosinophils and basophils 0%, lymphocytes 14%, monocytes 2%),

FIGURE 1. Aspect of the skin lesions in the dorsum.

platelets 224,000/mm³. Erythrocyte sedimentation rate (ESR) 7 mm. INR 1.03, prothrombin time 12.3 sec, albumin 3.4 g/dL, globulins 2.53 g/dL (α_1 0.26, α_2 0.51, β 0.68, γ 1.08 g/dL); glucose 104 mg/dL, urea 19 mg/dL, creatinine 0.9 mg/dL, sodium 137 mEq/L, potassium 4.2 mEq/L, magnesium 2.1 mEq/L, chloride 104 mEq/L, calcium 1.21 mmol/L; TSH 1.32 μ U/mL; antibodies antithyroglobulin negative, and antiperoxidase 10 U/mL; complement levels C3 134 mg/dL and C4 50 mg/dL; acid α_1 -glycoprotein 83 mg/dL. Rheumatoid factor and C-reactive protein titers were normal. Anti-Ro (SS-A) and anti-RNP were positive; anti-La (SS-B) and anti-Sm were negative; antibodies anticardiolipin IgM and IgG were positive and the lupus anticoagulant was negative. Hepatitis B and C and syphilis tests were negative. The urinalysis was normal. The cerebrospinal fluid (CSF) was clear, with 8 cells (neutrophils 51%, lymphocytes 47%, monocytes 2%); protein 90 mg/dL, glucose 57 mg/dL, chloride 123 mEq/L; serologic tests were negative for herpesvirus, cytomegalovirus, toxoplasmosis, syphilis, cysticercosis and schistosomiasis; Gram-stained smear and routine cultures resulted negative. The radiographic studies of the thorax, hands and knees revealed normal. The complete neuro-ophthalmologic evaluation resulted normal.

An electroneuromyography study showed absence of motor unities recruitment in the lower right limb, without signs of peripheral neuropathy. The uncontrasted computed tomography of thoracic spinal cord resulted normal, while in magnetic resonance imaging (MRI) the T2-weighted images after gadolinium disclosed multiple focal areas of hyper signal, aspect suggestive of spinal cord demyelinating neuropathy (Figure 2). Moreover, the nerve conduction evoked responses showed normal responses to visual and auditory stimuli, and dysfunction of the sensory fast conducting fibers mainly in right side of spinal topography. In addition, the T2-weighted and FLAIR images of the cranium with gadolinium revealed multiple bilateral focal areas of abnormal enhancement in the white matter, more conspicuously in the posterior parietal lobes and in the left temporal lobe, a finding compatible with demyelization and vasculitis (Figure 3).

FIGURE 2. T2-weighted images of MRI after gadolinium, showing multiple focal areas of hyper sign suggestive of demyelinating neuropathy in the spinal cord.

FIGURE 3. T2-weighted images of the cranium with gadolinium revealed multiple bilateral focal areas of abnormal enhancement in the white matter (encircled), compatible with demyelization and vasculitis.

The skin biopsy disclosed edema, lymphangiectasia, perivenular infiltrate predominantly of mononuclear cells, some degranulated mast cells and rare eosinophils (Figure 4). The direct immunofluorescence tests with IgA, IgG, IgM and C3 were negative and leukocytoclasia, fibrinoid necrosis and deposits of immunocomplexes were not found in the sample. The diagnoses of chronic urticaria and transverse myelitis associated with SLE were well established. The treatment for TM was initiated immediately after the establishment of this diagnosis, in order to halt eventual progression of cord compression, and consisted of pulse therapy with methylprednisolone (20 mg/kg/day) during five days, which resulted in rapid clinical improvement. The patient remains symptomless and she is under outpatient surveillance.

DISCUSSION

Although urticaria can not be considered among the diagnostic criteria for SLE, this condition may represent the first complain in persons that further have developed the classical features of SLE⁷. Our patient received prednisone for long-standing treatment of chronic urticaria, and presented SLE 26 years after the onset of the cutaneous lesions. More recently, she developed signs and symptoms indicative of myelopathy^{1,8,9} associated to SLE, characterized by acute bilateral signs and symptoms of motor disturbance and sphincter dysfunction; well defined upper level of sensory disturbance; elevated proteins and pleocytosis in CSF; exclusion of spinal cord compression by MRI; and progression to nadir into the period of 3 weeks after the onset of symptoms.

Neuropsychiatric changes occur in about 80% of patients with SLE; seizures and psychosis are diagnostic criteria and the most frequent features^{8,10}, in addition to anxiety and depression, dementia, deficit of cranial nerves, headache, peripheral neuropathy, cerebellar dysfunction, chorea, Guillain-Barré syndrome, strokes, aseptic meningitis, and myelopathy^{1,8,10}.

In this patient, the lupus anticoagulant was negative, and the anticardiolipin antibodies were positive. In general, the aPA may be detected in 30-50% of patients with SLE^{1,8}, while the inci-

FIGURA 4. High-power histopathologic aspect of skin disclosing edema, lymphangiectasia (asterisks), and perivenular infiltrate (arrowheads) predominantly of mononuclear cells.

dence of aPA in SLE patients with TM has been somewhat higher (55-64%)¹.

We emphasize the unusual long evolution (26 years) of skin changes before at least four diagnostic criteria for SLE could be fulfilled. Our patient showed 1) photosensitivity; 2) arthritis involving more than two peripheral joints; 3) immunologic disorder (IgG and IgM anticardiolipin, anti-RNP and anti-Ro antibodies); 4) antinuclear antibody in the absence of drug use; in addition to neurological disorders (aseptic meningitis and transverse myelitis)^{1,8,11}, and the chronic urticaria⁷. Brey et al (2002) found neuropsychiatric syndromes associated with SLE (NPSLE) in 80% of 128 patients¹⁰. Although aseptic meningitis and TM were not characterized in the subjects of that study, the roll of NPSLE syndromes includes aseptic meningitis and myelopathy^{1,8,11}.

With respect to urticaria, a possible concern could be the hypothesis of Schnitzler's syndrome (SS)¹², characterized by fever, arthritis and bone pains, associated with urticarial vasculitis (UV) due to autoimmune diseases as SLE. In fact, she presented skin lesions aggravated by sunlight and lasting more than 36 hours, in addition to aseptic meningitis and anti-Ro (SS-A) antibodies positive, suggesting the presence of UV^{4,7}. However, differing from this case, in SS occurs enlargement of

liver, spleen and lymph nodes, high ESR and globulin changes; moreover, UV is usually seen in patients with a more severe disease⁴, in which skin lesions characteristically show leukocytoclasia^{3,5}. Our report emphasizes the need of systematic diagnostic evaluations in patients with chronic

urticaria, because this condition constitutes a feature of some cutaneous vasculitis⁵, may antecede and can hinder the correct characterization of systemic diseases favouring diagnostic pitfalls, in special after long-standing treatment with corticosteroids.

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